

HL7 Drug Stability Reporting (eStability) Validation Procedures:

This document describes computer instructions for automating the validation of HL7 XML files for submission of drug stability reporting (eStability) data to FDA. Information on electronic submission may be found in guidance entitled *Providing Regulatory Submissions in Electronic Format – Drug Stability Reporting (eStability)*.

A link to the latest XML schema and controlled terminology used in Drug Stability Reporting (eStability) and other technical documents may be found on the FDA Data Standards Council web site at:

<http://www.fda.gov/ForIndustry/DataStandards/StabilityDataStandard/default.htm>.

Introduction

These validation procedures are for the use with the Health Level 7 (HL7) Stability Standard. This document describes the validation requirements needed for submitting information to the Food and Drug Administration (FDA) using the standard. This standard is meant to be used for all regulated product (e.g., test kits, drugs, reagents, medicated feeds, etc.), excluding foods. The Implementation Guide (IG) is based on the most up-to-date information from HL7 and should be used in conjunction with this document. The IG can be found on the FDA Data Standards Council web site at: <http://www.fda.gov/ForIndustry/DataStandards/StabilityDataStandard/default.htm>.

1. General

- 1.1. XML is well formed and valid against the schema, and any schematron rules embedded there in.
- 1.2. There are no data elements and attributes in addition to those described in this document (e.g., You can not create data elements and attributes that are not present in the schema).
- 1.3. There are no spaces in codes. Do not alter codes from the source. (e.g., C25158 is the code for Capsule, not C 25158).
- 1.4. All Ccodes do have a codeSystemName attribute. The only exception in the code for stabilityStudy for product when the official product name has not yet been established. When the official product name has been approved by the

FDA, use the NDC number (in the format of N followed by the NDC number in all numeral format) as the code content..

- 1.5. Display names are case insensitive.
- 1.6. There are no spaces in id extensions.
- 1.7. Letters in Globally Unique Identifiers (GUID) are lower case.
- 1.8. There are no empty or incomplete elements, except in certain circumstances, code, title, text, and time (an id has a root, a code has a code system).
- 1.9. Message header – This is not used by eStability. However an empty message header must be present for validation purpose. This is the current message header, refer to HL7 for required attributes:

```
<PORT_IN090004UV xmlns="urn:hl7-org:v3" xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
xsi:schemaLocation="urn:hl7-org:v3 C:\eStab_required\processable\multicacheschemas\PORT_IN090004UV.xsd"
ITSVersion="XML_1.0">
  <id/>
  <creationTime/>
  <interactionId/>
  <processingCode/>
  <processingModeCode/>
  <acceptAckCode/>
  <receiver typeCode="RCV">
    <device determinerCode="INSTANCE" classCode="DEV">
      <id/>
    </device>
  </receiver>
  <sender typeCode="SND">
    <device determinerCode="INSTANCE" classCode="DEV">
      <id/>
    </device>
  </sender>
```

- 1.10 When the eStability code list exists, must use the FDA preferred term in the exact case as shown in the code list. There are two code lists:

1.10.1 NCI Thesaurus

1.10.2 FDA Substance Registration List

2. XML references

The references indicate the character set, stylesheet, name space and schema.

- 2.1. The eStability file is defined in the PORT_HD090002UV02.xmd schema. However, this file contains only an abstract definition, and thus cannot be used directly for validation of the eStability file. By design, it is the “payload” of an HL7 message of the type PORT_IN090004UV02.

To correctly validate the eStability XML file, it is necessary to wrap it in a message header, though this may be completely empty, i.e. no real data has to be present inside the message header elements.

As there are likely to be many schemas, a path to the XML Schema should be stated in the xsi:schemaLocation attribute of the PORT_IN090004UV02 element, like:

```
<?xml version="1.0" encoding="UTF-8"?>
<PORT_IN090004UV02
```

xsi:schemaLocation="urn:hl7-org:v3
C:\HL7\v3ballot\html\processable\multicacheschemas\PORT_IN090004UV02.xsd"

- 2.2. XML reference is for version 1.0 and encoding "UTF-8".
- 2.3. There is an xml-styleSheet reference to <http://www.accessdata.fda.gov/stabilitydata/styleSheet/eStability.xsl>.
- 2.4. The schemaLocation of the urn:hl7-org:v3 namespace is provided as http://www.accessdata.fda.gov/stabilitydata/schema/multicacheschemas/PORT_IN090004UV02.xsd
- 2.5. There are no processing instructions other than the xml and xml-styleSheet declarations.
- 2.6. An eStability file has the extension ".xml".
- 2.7. The file name (excluding the path name) has to be alphanumeric, lower case (Electronic Common Technical Document (eCTD) restriction), and hyphens (no underscores and no blank spaces). The file name, including the extension, cannot exceed 64 characters.
- 2.8. Stability submissions consist of a stability message and/or associated stability message files. The sequence order of the messages is determined by the submitter.

3. Document information

This document discusses elements and attributes of the eStability message that have format constraints and/or reporting constraints based on the FDA business rules. Elements and attributes not mentioned are not changed and more information regarding them can be found in the Implementation Guide (IG). If the attribute or element is the only thing listed then it is mandatory based on FDA business rules.

- 3.1. controlActProcess - must have classCode="INFO" moodCode="EVN".
- 3.2. subject - must have a typeCode of typeCode="SUBJ".
- 3.3. StabilityStudy
 - 3.3.1. id
 1. id root is an Object Identifier (OID) <http://www.hl7.org/oid/> or alternatively a Globally Unique Identifier (GUID).
 2. id does not match any other id in the document.
 3. id is unique and can not be used as an id in other documents, sections and any other ids.
 - 3.3.2. reasoncode
 - 3.3.3. If the Data File Type is "Cycled-Complex", must also submit the associatedStudy XML file(s). See also 3.43.4.
- 3.4. ResearchSubject
 - 3.4.1. researchSponsor (Type: StudySponsor)

- 3.5. The subject of the study is a substance or a product, and is exactly one. An XML stability file is either for a "subjectProduct" or a "subjectSubstance", if it is for a "subjectSubstance" then there is no "specifiedIngredient".
 - 3.5.1. subjectSubstance
 - 1. expirationTime - The “approved” or “proposed” expiration period (e.g. 24 Months expressed using the width tag, see example code below) for the substance, or the existing expiration period for ongoing studies. This value works in conjunction with the “expirationTime” (3.17.3) in “ManufacturedMaterial” (3.17).
 - 3.5.2. subjectProduct
 - 1. expirationTime - The “approved” or “proposed” expiration period (e.g. 24 Months expressed using the width tag, see example code below) for the substance, or the existing expiration period for ongoing studies. This value works in conjunction with the “expirationTime” (3.17.3) in “ManufacturedMaterial” (3.17).
 - 2. specifiedIngredient
 - 3. The id number is constructed from the NDC number by prefixing it with “N”
- 3.6. SpecifiedIngredient
- 3.7. researchSponsor (Type: StudySponsor)
 - 3.7.1. id
 - 1. DUNS# format is nine digits (e.g., 12-345-6789 or 123456789).
 - 2. DUNS # is the primary identifier, it is listed first if multiple numbers are used.
 - 3. All numbers have a assigningAuthorityName
 - 4. The id number is constructed from the DUNS number by prefixing it with “D” and is constructed from the FEI number by prefixing it with “F”.
 - 3.7.2. name
 - 3.7.3. addr
 - 1. An address has a street address line, city, and country.
 - 2. Country is composed of letters only.
 - 3. If the country is “USA”, then the contact party has a state and postal code.

4. If the country is “USA”, then the postal code is 5 digits with optionally a dash followed by 4 numbers.
 5. If the country is **not** in the postal code validation list, then there must be a postal code. The postal code list is in the downloadable terminology files "Additional Validation Files" and the file name is “postal_codes_val.xml” located on this web page:
<http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm169455.htm>,. We utilize this list to determine whether or not a country has a postal code system when validating drug establishment registration submissions.
- 3.8. Specification
- 3.8.1. code
Display name.
 - 3.8.2. text
 - 3.8.3. component (Type: Component6)
- 3.9. component (Type: Component6)
- 3.10. TestDefinition - Check that there are no Level 3 Test Definitions.
- 3.10.1. id
 1. id root is an Object Identifier (OID) <http://www.hl7.org/oid/> or alternatively a Globally Unique Identifier (GUID).
 2. id does not match any other id in the document except in a reference stub.
 3. All test OID’s are unique (subjectOf/specification/testDefinition).
 4. All test OID’s are defined in subjectOf/specification/testDefinition, i.e., no test OID is an orphan (component1/testing/component/definition/definitionStub/id).
 - 3.10.2. code
 - 3.10.3. text
 - 3.10.4. methodCode
 - 3.10.5. referenceRange
 - 3.10.6. component (Type: Component7)
 1. If there is only a first level test, then there is no Component7.
 2. If there are two levels of test, at level one there is no pause quantity or sequence number.

3. There is a pause quantity or sequence number at level 2.
- 3.11. code
 - 3.11.1. code
 1. Code system is 2.16.840.1.113883.3.26.1.1.
 2. Code comes from the Document type list.
 3. Display name matches the code.
 - 3.11.2. originalText
 1. The test name
- 3.12. methodCode
 - 3.12.1. code
 1. Code system is 2.16.840.1.113883.3.26.1.1.
 2. Code comes from the Document type list.
 3. Display name matches the code.
 - 3.12.2. originalText
 1. The test method, or test SOP
- 3.13. referenceRange
 - 3.13.1. acceptanceCriterion
- 3.14. AcceptanceCriterion
- 3.15. component (Type: Component5)
- 3.16. StudyOnBatch
 - 3.16.1. id
 1. id root is an Object Identifier (OID) <http://www.hl7.org/oid/> or alternatively a Globally Unique Identifier (GUID).
 2. id does not match any other id in the document.
 - 3.16.2. code
 1. displayName must indicate the type of study (Commercial, Clinical, etc.).
 2. In the future this will be connected to a code list and will be updated when this occurs.
- 3.17. subject (Type: Subject2)
- 3.18. Instance
- 3.19. ManufacturedMaterail
 - 3.19.1. existenceTime

1. There is an existence time with at least the precision of day in the format YYYYMMDD, that all effective times and expiration times in the file must be later than.
- 3.19.2. lotNumberText
- 3.19.3. expirationTime
 1. Must have a 'low value' (for Proposed) or a 'high value' (for Approved). This value works in conjunction with the "expirationTime" (3.5.1.1 and 3.5.2.1) in "subjectProduct" (3.5.1) or "subjectSubstance" (3.5.2)..
- 3.20. asManufacturedProduct (Type: ManufacturedProduct)
- 3.21. Manufacturer
 - 3.21.1. id
 1. DUNS# format is nine digits (e.g., 12-345-6789 or 123456789).
 2. DUNS # is the primary identifier, it is listed first if multiple numbers are used.
 3. All numbers have a assigningAuthorityName
 4. The id number is constructed from the DUNS number by prefixing it with “D” and is constructed from the FEI number by prefixing it with “F”.
 - 3.21.2. name
 - 3.21.3. addr
 1. An address has a street address line, city, and country.
 2. Country is composed of letters only.
 3. If the country is “USA”, then the contact party has a state and postal code.
 4. If the country is “USA”, then the postal code is 5 digits with optionally a dash followed by 4 numbers.
 5. If the country is not in the *postal code validation list*, then there is no post code.
 - 3.21.4. assignedEntity (Type: AssignedEntity2)
 1. If you are using a sub contractor you need to have an assignedEntity element that has a representedManufactured child element that follows the same rules as 3.21 above.
- 3.22. content (Type: asContent)
- 3.23. Container

- 3.23.1. code
 - 1. Code system is 2.16.840.1.113883.3.26.1.1.
 - 2. Code comes from the Document type list.
 - 3. Display name matches the code.
- 3.23.2 capTypeCode
 - 1. displayName must indicate the type of cap.
 - 2. In the future this will be connected to a code list and will be updated when this occurs.
- 3.24. BatchIngredient
- 3.25. component1 (Type: Component3)
 - 3.25.1. pauseQuantity
- 3.26. Testing
 - 3.26.1. effectiveTime
 - 1. There is an effective time with at least the precision of day in the format YYYYMMDD.
- 3.27. performer (Type: Performer1)
- 3.28. AssignedEntity
- 3.29. assignedTestingSite (Type: TestingSite)
 - 3.29.1. id
 - 1. DUNS# format is nine digits (e.g., 12-345-6789 or 123456789).
 - 2. DUNS # is the primary identifier, it is listed first if multiple numbers are used.
 - 3. All numbers have a assigningAuthorityName
 - 4. The id number is constructed from the DUNS number by prefixing it with “D” and is constructed from the FEI number by prefixing it with “F”.
 - 3.29.2. name
 - 3.29.3. addr
 - 1. An address has a street address line, city, and country.
 - 2. Country is composed of letters only.
 - 3. If the country is “USA”, then the contact party has a state and postal code.
 - 4. If the country is “USA”, then the postal code is 5 digits with optionally a dash followed by 4 numbers.

5. If the country is not in the *postal code validation list*, then there is not a post code.
- 3.30. component (Type: Component1)
 - 3.30.1. test
- 3.31. Test
 1. There can be many Tests for a TestDefinition; these are replicate analysis.
 - 3.31.1. title
 - 3.31.2. definition
- 3.32. performer (Type: Performer2)
 1. Must have a typeCode of typeCode="PRF".
- 3.33. AssignedEntityStub
- 3.34. assignedSiteStud
 - 3.34.1. id
 1. DUNS# format is nine digits (e.g., 12-345-6789 or 123456789).
 2. DUNS # is the primary identifier, it is listed first if multiple numbers are used.
 3. All numbers have a assigningAuthorityName
 4. The id number is constructed from the DUNS number by prefixing it with "D" and is constructed from the FEI number by prefixing it with "F".
- 3.35. Definition
- 3.36. DefinitionStub
 - 3.36.1. id
 1. id root is an Object Identifier (OID) <http://www.hl7.org/oid/> or alternatively a Globally Unique Identifier (GUID).
 2. id does match an id in the specification section of the document.
- 3.37. Component (Type: Component2)
 1. This is the stability data for the second level test.
 - 3.37.1. sequenceNumber
 - 3.37.2. pauseQuantity
 - 3.37.3. test
- 3.38. componenet (Type: Component4)

- 3.39. Storage
 - 3.39.1. effectiveTime
 - 1. There is an effective time with at least the precision of day in the format YYYYMMDD.
- 3.40. ControlVariable
- 3.41. StorageCondition
- 3.42. componentOf (Type: Component)
 - 1. Must have a typeCode of typeCode="COMP".
- 3.42.1. sequenceNumber
- 3.43. AssociatedStudy - Check that referenced associated files are there
 - 3.43.1. id
 - 1. id references that of another stability message (associated study) in the same submission.
 - 2. id root is an Object Identifier (OID) <http://www.hl7.org/oid/> or alternatively a Globally Unique Identifier (GUID).
 - 3. id does not match any other id in the document.
 - 3.43.2. text
 - 3.43.3. If the XML file references AssociatedStudy(s), all the XML files must be contained in the same folder of zip archive.
 - 3.43.4. If the Data file Type is 'Cycled-Complex', must submit the accompanying associatedStudy files. See also 3.3.3.

Version History

Version	Date	Comments
0.1	12-DEC-2011	Original
0.2	25-FEB-2013	Corrected the identifier, inserted new table design